Bram Rochwerg, MD, MSc (Epi), FRCPC, Series Editor

The Ins and Outs of IV Fluids in Hemodynamic Resuscitation

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David A. Kaufman, MD[1]
Marcela Lopes, MD[2]
Niharika Maviya, BS[3]
Sheldon A. Magder, MD[4]

OBJECTIVES: Concise definitive review of the physiology of IV fluid (IVF) use in critically ill patients.

DATA SOURCES: Available literature on PubMed and MEDLINE databases.

STUDY SELECTION: Basic physiology studies, observational studies, clinical trials, and reviews addressing the physiology of IVF and their use in the critically ill were included.

DATA EXTRACTION: None.

DATA SYNTHESIS: We combine clinical and physiologic studies to form a framework for understanding rational and science-based use of fluids and electrolytes.

CONCLUSIONS: IVF administration is among the most common interventions for critically ill patients. IVF can be classified as crystalloids or colloids, and most crystalloids are sodium salts. They are frequently used to improve hemodynamics during shock states. Many recent clinical trials have sought to understand which kind of IVF might lead to better patient outcomes, especially in sepsis. Rational use of IVF rests on understanding the physiology of the shock state and what to expect IVF will act in those settings. Many questions remain unanswered, and future research should include a physiologic understanding of IVF in study design.

KEY WORDS: colloid; crystalloid; fluid responsiveness; intravenous fluids; resuscitation

Administration of IV fluids (IVF) is one of the most common clinical interventions in hospitalized patients, first described nearly 200 years ago (1). Use of IVF ranges from the provision of fluids for daily needs in patients who cannot drink to the treatment of shock. Wise use of IVF depends on understanding how they can be expected to distribute in the body and their physiologic function in homeostasis. The use of IVF for shock resuscitation, recent developments in monitoring IVF effects, and recent IVF clinical trials are discussed in excellent recent reviews and we refer readers to those studies for a complete discussion of those aspects (2–4). In this concise definitive review, we take a complementary approach, discussing basic physiologic principles underpinning body fluids and how to use those principles to guide IVF prescription, with a focus on adult physiology. Similar principles apply in pediatric physiology (5).

PHYSIOLOGIC BACKGROUND: WHAT FLUIDS DO IN THE BODY

In the normal state, 50% or more of the body is composed of a solution of salts and water. The composition of the salt solutions varies among body compartments, but they are all close to 1% salt solutions (6). Body fluids have two main functions. First, they dissolve essential substrates, allowing them to move

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KEY POINTS

Question: What is the physiologic foundation for using IV fluids (IVF) in a critically ill patient?

Findings: IVF distribute among body compartments according to the biochemistry of each compartment, the composition of the IVF administered, and the underlying pathophysiology of the individual patient.

Meaning: Using IVF for critically ill patients wisely requires an understanding of how IVF influences hemodynamics and the water and electrolyte state of each body compartment.

by diffusion. Second, fluids allow the substances they contain to flow by convection through the circulatory and lymphatic systems.

Particles dissolved in water form solvation structures with water molecules. This interaction creates a force, osmotic pressure, which is determined by the number of dissolved particles, regardless of their size or charge. This force is measured as "osmolarity" (Osm/kg) or "osmolality" (Osm/L). "Tonicity" describes how the osmolalities of two solutions on either side of a semipermeable membrane compare with each other. Pragmatically it can be based on whether an RBC with normal osmolality shrinks or expands when it is placed in a solution. **Table 1** summarizes key concepts about osmolality, osmolarity, and tonicity (5, 7). A fundamental principle governing the movement of body fluids is the principle of iso-osmolality. With a small exception discussed below, all body compartments have the same osmolality. If the membrane separating two compartments is permeable to water, water moves to the region with a higher osmolality until equilibrium is achieved. Normal osmolality of body compartments is 275–295 mOsm/L. Sodium is the dominant osmole in the extracellular compartment, and its concentration is tightly regulated at 135–145 mMol/L. Furthermore, by regulating sodium, negative ions also are regulated to maintain electrical neutrality. Elements cannot be metabolized. Thus, their total amounts in the body ("not" their concentration) are determined by absorption and excretion. Because of this, the amount of sodium in the body is the primary determinant of body water. Fluid excess means excess body sodium and fluid depletion means reduced total body sodium.

Under normal conditions, approximately two-thirds of total body water is intracellular and one-third is extracellular (**Fig. 1**) (6). The extracellular compartment is further divided into the intravascular and interstitial spaces, and the volume of the interstitial space is typically twice that of the intravascular space. An exception to the principle of iso-osmolality is crucial: the osmolarity of plasma is ~ 1 mOsm/L greater than the body's other compartments because vascular walls are relatively impermeable to plasma proteins and other large molecules. This small difference in osmotic pressure maintains extra plasma water. Substances that act like this are called colloids and this type of osmotic pressure is called oncotic pressure. Albumin accounts for close to 80% of plasma oncotic pressure and thus produces the major force retaining fluid in the vascular space.

Flux of fluid between the vascular and interstitial spaces is governed by opposing forces first described by Starling (**Fig. 2**) (8). Hydrostatic pressure is higher inside blood vessels than outside, favoring fluid flux from the vascular to the interstitial compartment. In contrast, the oncotic pressure in the vascular space (mainly from albumin) is higher than in the interstitial space, resisting outward fluid flux. Starling believed that fluid moves out of the vessels at the beginning of capillaries and is reabsorbed at the end. Recent studies

TABLE 1.
Summary of Commonly Used Terms That Describe Physiologic Solutions

Term	Definition
Osmolality	The concentration of a solution expressed as the total number of solute particles per kilogram of solvent
Osmolarity	The concentration of a solution expressed as the total number of solute particles per liter of solvent
Tonicity	The effective osmotic pressure gradient created by dissolved particles that cannot cross a semipermeable cell membrane

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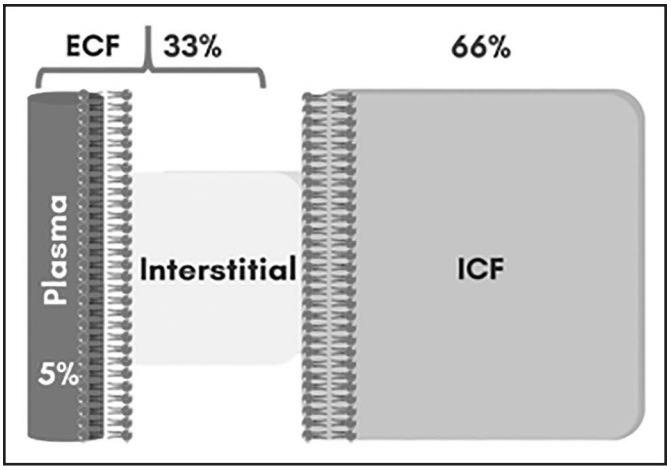

Figure 1. A schematic model of fluid compartments in the human body. Typically, two-thirds of body water is in the intracellular fluid (ICF), where potassium is the osmole that regulates its volume. One-third of body water is in the extracellular fluid (ECF), where sodium is 1 the osmole that regulates extracellular volume. The extracellular compartment is further divided into the interstitial and intravascular spaces. Under normal circumstances, the interstitial fluid volume is twice that of the intravascular fluid volume.

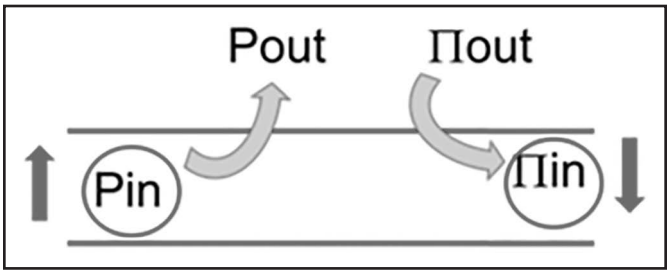

Figure 2. The Starling model of fluid flux between the intravascular and interstitial space describes the fluid flux across a porous or semipermeable membrane (64).$Jv/A = L_p[(P_{in}-P_{out})-\sigma(\varpi_{in}-\varpi_{out})]$.$Jv/A$ is the fluid flux across the membrane (where A is the surface area), L_p is the hydraulic conductance constant (which describes the ease with which a fluid moves across a porous membrane), P_{in} is the vessel hydrostatic pressure, P_{out} is the interstitial hydrostatic pressure, σ is the reflection coefficient (which describes the ease with which a particle moves across the porous membrane), ϖ_{in} is the oncotic pressure inside the vessel and ϖ_{out} is the oncotic pressure outside the vessel. In Starling's original version, ϖ_{out} was negligible but in the updated version ϖ_{out} can be more than 50% of ϖ_{in} and varies with the filtration rate; it thus requires a more complex equation. Effective ϖ_{out} also now thought to be based on the oncotic pressure within the glycocalyx rather than in the interstitium. As a result, except when there is a marked fall in P_{in}, fluid filtration in capillaries is always outward and fluid returns to the vasculature through lymph flow.

indicate that in the steady state, in most tissues there usually is net flux of fluid into the interstitial space and that the lymphatics return this volume to the vasculature via the great veins, except when there is severe acute loss of vascular volume (9). Starling also assumed that interstitial albumin concentration was negligible but it actually is about 50% of the vascular concentration (9, 10). Starling's law has been revised by the discovery of the glycocalyx: current models suggest that oncotic pressure within the glycocalyx (rather than the interstitial fluid) regulates filtration (9, 10). Pathologic changes to the glycocalyx and their effects on fluid physiology have been the focus of much recent investigation (11–13).

Three types of fluid are used clinically: crystalloids, colloids, and plasma (14, 15). Patterns of IVF use vary widely around the world (16). Packed erythrocytes or platelets add cellular mass (and volume) to the vascular space but not osmoles, so we omit them from this concise review. Characteristics of commonly infused fluids are listed in **Table (ESM)** (http://links.lww.com/CCM/H380). Almost all crystalloid IVF are sodium salts in water; an exception is dextrose in water (15). The most common is 0.9% NaCl. Its sodium concentration is 154 mMol/L (3.5 g sodium), which decreases when mixed with serum. The chloride concentration, too, is 154 mMol/L, which is much higher than that of plasma. Kidneys are less effective at excreting chloride than sodium, so large infusions of 0.9% saline can produce hyperchloremic metabolic acidosis. To reduce the chloride content, other anions are used, including lactate, acetate, or gluconate in what is called "balanced" solutions (17). Colloid solutions contain large molecular weight (MW) molecules dissolved in a crystalloid solution, which usually is 0.9% NaCl. These large MW particles are too large to cross the vascular wall easily and thus remain primarily inside the vascular space until they are metabolized (Fig. 2). The most common colloids are proteins and hydroxyethyl starches. Infused proteins are albumin (derived from human plasma) or gelatins (from animal sources). Albumin comes as a 4% or 5% solution, which has oncotic effects close to that of normal plasma, or 20% or 25% solutions, which are hyperoncontic. Starches are complexes of either dextran or hydroxyethyl starches (known as hetastarch), which have been modified to alter their rate of breakdown by serum amylase. Their oncotic values, therefore, vary because it is particle number that determines osmotic force. In the United States, hetastarchs carry a Food and Drug Administration-mandated black box warning because their use has been associated with increased risk of death in patients with sepsis (18).

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Under pathologic conditions fluid can accumulate in body compartments that do not normally contain much fluid and whose fluid is not readily available to the circulatory system, often called "third spaces." Major third spaces include the peritoneal cavity and pleural space. Based on the principle of iso-osmolality, the solute concentrations in these spaces must equilibrate with the rest of the extracellular fluid (ECF) (19). This has important implications for clinical use of crystalloid infusions. Under normal circumstances, infused isotonic crystalloid solutions distribute approximately one-third into the vascular space and two-thirds into the interstitial space. However, when the interstitial and third spaces are greatly expanded (e.g., by edema, ascites, or pleural effusions) the proportion of infused crystalloids and their electrolytes distribute evenly into all of these regions, and the fraction remaining in the plasma is reduced proportionally. Excess fluid accumulation in the interstitial and "third" spaces theoretically may cause organ edema and disrupt interactions between cells and tissues (20). Signs of venous congestion have been associated with an increased risk of acute kidney injury in large ICU databases (21). Venous congestion will also be expected to slow lymphatic return of fluid to the intravascular space, as lymphatics are low-pressure vessels that drain into veins.

Interstitial sodium and water provide a reserve that can be recruited into the vascular space to restore plasma volume when there is an acute fall in intracapillary pressure. The interstitial space also can take up the volume from the vascular space and buffer excess vascular volume. Consider what occurs in patients undergoing hemodialysis. They commonly have around 4 L of fluid removed during a 3–4 hour dialysis session without adverse effects. As plasma water and sodium are ultrafiltered, they are replaced by reserves from the interstitial space. When the interstitial volume expands, interstitial structure changes and allows more volume uptake with small changes in pressure. In this sense, edema begets more edema when excess IVF is given (6).

The other major volume reserve is the unstressed vascular volume. About 70% of blood volume rounds out vessel walls and does not contribute to vascular pressure (22–24). The other 30% of vascular volume stretches the wall of vessels, creating elastic recoil of vessel walls, and generating vascular pressure. This 30% is called the stressed vascular volume. (**Fig. 3**) Discharge from the sympathetic nervous system (or exogenous catecholamines) can induce contraction of vascular smooth muscle, recruiting more unstressed volume into stressed volume, which occurs in seconds (24–26).

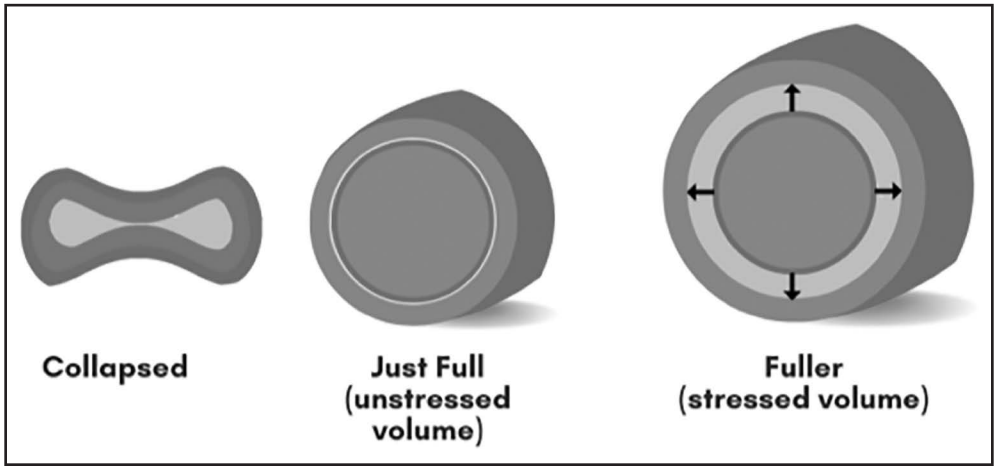

Figure 3. The effects of intravascular volume on vascular tone and elastic recoil. In typical conditions, vessels, especially veins, are just full (they are at the limit of their unstressed volume). The elastic recoil of the vein wall does not contribute a great deal to venous return of blood to the heart. When veins are fuller and they are beyond their unstressed volume, the intravascular volume contributes to the stressed volume, stretching the vessel wall, and the elastic recoil properties of the veins play an important role in generating venous return of blood to the heart. In volume depletion, or in situations with elevated pressure outside the veins, the veins tend to collapse, and the veins become resistors, impeding venous return of blood to the heart.

MOVEMENT OF FLUIDS–WATER, NORMAL SALINE, HYPERTONIC SALINE, AND COLLOID

With IVF infusion into the vasculature, two things happen: 1) the vascular walls are stretched, increasing intravascular pressure, and 2) the concentration of solutes in the vascular space changes relative to the interstitial and intracellular spaces. A solution of 5% dextrose in water is isotonic (it will not lyse erythrocytes) but the dextrose is rapidly taken up by cells and metabolized,

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leaving pure water. The solute concentration of the intravascular fluid falls relative to that of the interstitial fluid. The resulting change in the concentration gradient causes water to move into the interstitial space. Interstitial fluid is diluted in comparison to the intracellular fluid, and water then moves into cells. The infused water is thus distributed among all three fluid compartments.

Infusing an isotonic crystalloid such as 0.9% saline changes the solute concentration in the vascular space. Salt and water equilibrate with interstitial fluid. If the final osmolality of the vascular and interstitial spaces is unchanged; the fluid does not enter cells. An infusion of 5% albumin (5 g per 100 mL of 0.9% NaCl) is iso-oncotic and iso-osmotic with normal plasma and should remain in the vascular space until the albumin is metabolized or filtered from the vascular space into the interstitial space, which happens more quickly when the capillary filtration reflection coefficient is low. When albumin enters the interstitial space, a new equilibrium between interstitial and plasma oncotic pressure is established, and much of the filtered albumin eventually returns to the plasma via lymphatics (27). Twenty-five percent albumin has an oncotic pressure that is much higher than that of plasma and limits to flux of water into the interstitial space from the intravascular space; in situations when the vascular hydrostatic pressure is low, hyperoncotic albumin may draw fluid and electrolytes back from the interstitium, expanding the former (9, 28). Infusions of hypertonic crystalloids (such as 3% or 5% NaCl) expand intravascular volume and shrink the interstitial space and the intracellular space but eventually, a new equilibrium among the fluid compartments will be achieved, according to the principle of iso-osmolarity (see above).

CIRCULATING BLOOD VOLUME

The second major role of body fluids is the creation of vascular pressures. The difference in vascular pressures among compartments allows the distribution of blood to tissues. Blood flow is determined by two functions: 1) the venous return function, which is based on parameters that drive blood from the systemic veins to the heart, and 2) the cardiac function, based on the parameters of the heart as a pump.

As Guyton described, the large blood volume in the compliant systemic veins creates a pressure called mean systemic filling pressure (MSFP) that drives volume back to the right atrium (29). Cardiac function, described by Starling curves, depends upon the volume stretching the heart in diastole (preload), afterload, contractility, and heart rate (30). The primary role of the heart is permissive; by rhythmically lowering right atrial pressure, venous blood drains from systemic veins back into the heart. The heart also is restorative; it returns blood to the systemic veins generating the systolic blood pressure that distributes flow through regional circulations. Cardiac output (CO) is determined by the intersection of these two functions: CO must match cardiac input in a steady state.

These functions have important limits. When the pressure in the great veins is less than the surrounding intrathoracic pressure they collapse as they enter the chest which limits venous return to the right atrium. Flow back to the heart can then only increase if MSFP increases or venous resistance decreases. The only way volume increases CO is by increasing MSFP and cardiac preload. The end-diastolic volume of the right ventricle is limited by the size of the pericardial sac and the maximum diastolic volume of the heart. Increasing end-diastolic pressure beyond these limits will not increase end-diastolic volume or stroke volume. CO then can only increase by increasing heart rate or cardiac contractility or by decreasing ventricular afterload. Another important limitation of IVF administration is venous congestion. As venous pressure rises, lymphatic drainage may decline, resulting in reduced clearance of interstitial fluid. Also, raising the venous pressure without raising CO or arterial blood pressure will reduce organ perfusion pressure, potentially worsening organ perfusion and function (31).

PHYSIOLOGICALLY BASED CLINICAL USES OF IVF

Hypovolemia Due to Hemorrhage

Pathophysiology. In the first stage of bleeding, plasma, platelets, and erythrocytes are lost, vessels are underfilled, and CO and vascular pressures fall. This triggers baroreceptor activation, leading to sympathetic discharge, which increases systemic vascular resistance to maintain blood pressure. Hemorrhage also decreases vascular capacitance, which recruits unstressed volume into stressed volume, effectively generating an autotransfusion, thereby increasing venous return,

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ventricular stroke volume, and CO (25). Decreased intravascular hydrostatic pressure results in less flux of fluid from the vasculature to the interstitial space. When hemorrhage is severe, fluid can move from the interstitial space to the intravascular space, which helps maintain CO (9). Hemoglobin concentration decreases due to dilution from the influx of interstitial fluid, offsetting some of the increase in oxygen delivery that results from increased CO. How much compensation occurs depends on the available reserves in unstressed intravascular volume and interstitial volume and how much an individual can respond with increased sympathetic activation.

Rationale. The primary goals of resuscitation of hemorrhage are 1) to find the source of bleeding, 2) to stop the hemorrhage, and 3) to replace the blood components that were lost. Although IVF may increase CO, depending on the balance between the increase in CO and decrease in hemoglobin concentration, oxygen delivery potentially could fall even though there may be a comforting increase in arterial blood pressure (32). Thus, IVF must be used cautiously in hemorrhagic shock. Furthermore, increasing vascular pressures can disrupt hemostatic clots and increase hemorrhage. Trauma guidelines emphasize hemostatic, hypotensive resuscitation, with blood components favored over crystalloids to provide a combination of volume resuscitation and hemostasis with targeting low blood pressures before damage control surgery (33).

Hypovolemia Due to Nonhemorrhagic Volume Loss

Pathophysiology. Body fluid volume is regulated by the total amount (not concentration) of sodium in the body, so volume loss is sodium loss. Sodium and water need to be provided to replace lost fluid and restore intravascular and interstitial volume.

Rationale. Isotonic crystalloid solutions refill stressed and unstressed vascular volume and the interstitial space. In moderate amounts, 0.9% saline is appropriate for most patients. However, clinicians should monitor plasma chloride concentration when large amounts of chloride-rich solutions are infused because elevated chloride concentration relative to sodium produces metabolic acidosis (34). The kidneys also are much less effective at clearing chloride than sodium. When plasma chloride concentration increases, clinicians should consider crystalloids with lower chloride content. This is especially important in patients who have renal tubular dysfunction (such as due to diabetes mellitus or hypertension). Intracellular volume is protected by cells' ability to regulate their intracellular electrolyte content by losing intracellular water, making organic solutes (idiogenic osmoles), or binding intracellular ions when ECF osmolality changes (35). Idiogenic osmoles are metabolized and intracellular water is released as the osmolality of the extracellular compartment returns to normal (36, 37). Note that the stressed volume and thus CO and vital signs can be normal even though unstressed volume is markedly decreased. The clinical history and physical examination can give important clues (38, 39). Colloid solutions do not play an important role in the management of shock from hypovolemia.

High-profile studies have tested the hypothesis that the use of lower chloride solutions is beneficial. In general, large clinical benefits have not been found but the total infused volume and the amount of chloride have been too low to test the hypothesis effectively. These studies also were not enriched with higher-risk populations, such as those with renal tubular dysfunction. In the one study that showed a small benefit, chloride concentration was not monitored or treated, so the benefit could have been because of the failure to provide optimal care to the control group (40–42). Using up to 2 L of 0.9% saline is unlikely to be harmful but with higher infused volumes, plasma chloride concentration should be monitored closely. Future studies should test the chloride hypothesis in higher-risk populations. Overnight nil per os (npo) periods are not likely to be associated with substantial increases in perioperative IVF needs (43).

Distributive Shock: Decreased Vascular Tone and Increased Vascular Leak

Pathophysiology. Disorders such as anaphylaxis, neurologic injury, or severe inflammation (sepsis, pancreatitis) increase vascular permeability and decrease vascular tone, resulting in diminished venous return (loss of water and solute from the plasma and venodilation) and arterial vasodilation, both of which may cause low blood pressure. Preload is inadequate to maintain the CO required by increased metabolism and maldistribution of arterial blood flow and IVF are often administered to try to increase CO and tissue perfusion.

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Rationale. IVF infusion can potentially increase SV and CO by increasing stressed volume, increasing MSFP and venous return to the heart but only as long as the heart is operating on the ascending part of the Starling curve (**Fig. 4**) (29, 30, 44). On the flat part of the curve, IVF infusion only raises right ventricular end-diastolic "pressure" and not end-diastolic "volume" so the SV is unchanged. The blood pressure is already low so afterload reduction to increase CO is contraindicated. Only an increase in heart rate or contractility can raise CO. Various clinical tests of fluid responsiveness (FR) may help clinicians determine whether the patient is on the ascending of the Starling curve, as reviewed elsewhere, and these tests may help clinicians make decisions about IVF administration (2, 45). Using FR to guide IVF in sepsis has been associated with lower morbidity and mortality (46–48).

An increase in venous return with crystalloids inevitably increases vascular leak because vascular hydrostatic pressure increases and plasma oncotic pressure decreases. Colloids can potentially reduce the volume of IVF needed to increase stressed volume but leak into the interstitial space, especially when vascular permeability is high. The amount of leakage is lower during hypovolemia; if albumin is the colloid, leaked albumin can return to the plasma via lymphatics, if it is not broken down in the interstitium (27, 49). Catecholamines and arginine vasopressin (and its analogs) can potentially restore arterial pressure. The increase in arterial resistance can lower capillary pressures, thereby reducing vascular leaks. Norepinephrine also increases cardiac contractility and venous return. There is evidence that the use of norepinephrine is associated with fewer adverse effects than dopamine and norepinephrine is recommended as the first-line vasopressor for septic shock (26, 50, 51). Hyperoncotic albumin (25%) can potentially retrieve interstitial fluid back into the vascular space; however, if vascular permeability to proteins is high, albumin may leak into the interstitial space (28).

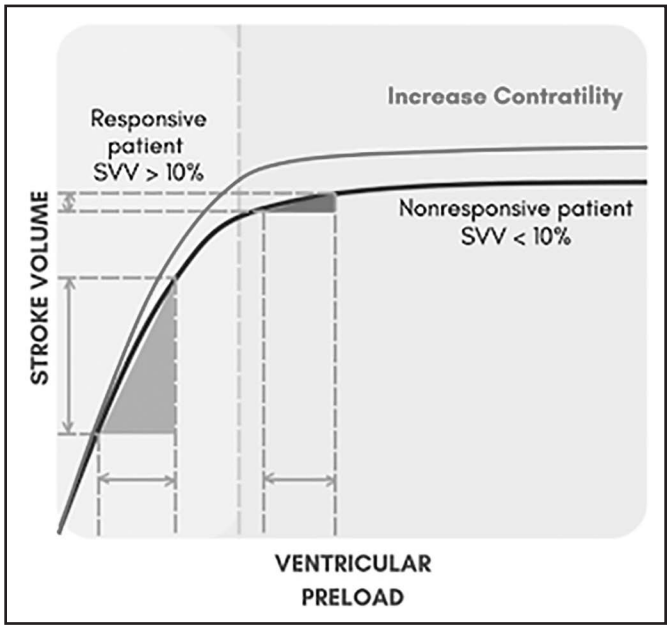

Figure 4. Starling curves. These curves describe the effects of increasing preload (end-diastolic volume) on stroke volume. If heart function is described by the ascending part of the curve, adding preload will increase stroke volume (fluid responsiveness, *larger left triangle*). If the flatter part of the curve describes heart function, adding preload will not appreciably increase stroke volume (fluid unresponsiveness, *smaller left triangle*). Increases in contractility (the *upper Starling curve*) shift the curve upwards and to the left, and fluid responsiveness occurs at a higher preload, making the patient more fluid responsive. Similarly, lower contractility (*curve not shown*) will shift the Starling curve downward and to the right, and fluid responsiveness will disappear at a lower preload, making a patient less fluid-responsive.

Sepsis is the commonest cause of distributive shock (50). The role of IVF in sepsis resuscitation is controversial. In one highly cited, single-center, unblinded study, mortality was substantially reduced with a protocol aimed at optimizing oxygen delivery early in the course of septic shock (52). Expert guidelines gave a "strong recommendation" to give at least 30 mL/kg of IV crystalloids for patients with sepsis and hypoperfusion despite a low quality of evidence (53). Three subsequent large, multicenter randomized controlled trials did not replicate the mortality benefit from the initial single-center study (54–56). Two studies of early IVF resuscitation for sepsis in low-resource settings found IVF loading to be associated with increased mortality (57, 58). A retrospective study of "sepsis bundles" found no association between early IVF and reduced risk of death (59). In the 2021 Surviving Sepsis Guidelines, the recommendation for IVF resuscitation was downgraded to "weak" (51).

A clinical and individualized approach combining the history, physical examination, laboratory analyses, reliable monitoring tools, and iterative assessment of circulatory parameters to individualize IVF and vasopressor resuscitation is likely to lead to better outcomes than algorithms (60). A recent small prospective study and two retrospective studies suggest that using CO monitoring to guide IVF

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administration in sepsis may be associated with lower morbidity and mortality (46–48). Future prospective studies might focus on this area.

Two recent randomized controlled trials compared the liberal use of IVF to the restrictive use of IVF plus the early use of vasopressors in septic shock patients (61, 62). In both studies, the total volume of infused IVF was lower in the restrictive IVF/early vasopressor group, and the risk of death was similar with both interventions. In both studies, the infused IVF volume (under 2 L) was lower than in older studies (52, 54–56). One interpretation of the accumulated observations is that large volumes of IVF are not needed, which is consistent with their limited role in raising CO, whereas moderate volumes of IVF do not seem to be harmful, possibly because they fill depleted reserves (see discussion of hypovolemia due to nonhemorrhagic volume loss, above.)

Cardiogenic and Obstructive Shock: The Pump Is Broken or Blocked

Pathophysiology. Cardiac dysfunction, due to myocardial depression or increased ventricular afterload loads (pulmonary embolism, cardiac tamponade) raises intracardiac and central venous pressures to the point of a loss of FR (Fig. 4). With left ventricular failure, volume and pressure rise in the pulmonary vasculature, resulting in pulmonary edema, hypoxemia, and increased work of breathing before the RV volume limit is reached. The resulting hypoxemia and acidemia lead to global cardiac failure with signs of hypervolemia and venous congestion. IVF will not increase CO. Similarly, IVF rarely has value in shock caused by pulmonary embolism: shock occurs because RV filling has reached its physical limit (61, 62). In tamponade, volume can temporarily increase SV by countering the pressure surrounding the heart but it is not sustainable and results in organ congestion.

Rationale. IVF has little role in the management of cardiogenic or obstructive shock because the shock is due to the physical limitation of RV filling (63). Treatments should be aimed at restoring ventricular function either with inotropic agents, mechanical devices, or relief of obstruction (thrombolysis, removal of pericardial effusion). IVF may contribute to RV dysfunction or contribute to congestion of vital organs, which, combined with decreased perfusion pressure, causes organ dysfunction. RV dysfunction and limitation were recently reviewed elsewhere (63).

CONCLUSIONS

Although resuscitation with IVF is common, their benefit is not always clear and many knowledge gaps exist. When prescribing IVF, physicians should consider the physiologic roles of fluids and how IVF use will fix the pathophysiology underlying the clinical problem. The primary goal of IVF is to increase CO and oxygen delivery. If CO is not volume responsive, IVF's only role is to restore depleted volume reserves. A second role of IVF is to restore perfusion pressure and thereby allow better distribution of flow. This, too, can only occur by increasing CO and does not occur when the heart is functioning on the flat portion of its function curve. Furthermore, clinicians should keep in mind that arterial blood pressure is an unreliable surrogate for blood flow and oxygen delivery. Thus, increasing CO while at the same time reducing arterial oxygen content does not improve tissue oxygenation. Finally, the type of IVF chosen should depend on the pathology of the process being treated and not on the characteristics of IVF itself. Future research should focus on including these principles in the design of trials aimed at testing hypotheses regarding the utility of different IVF prescriptions for shock.

1 *Division of Pulmonary and Critical Care Medicine, NYU Grossman School of Medicine, New York, NY.*

2 *Intensive Care Unit, Hospital da Cidade, Salvador, Bahia, Brazil.*

3 *Albert Einstein College of Medicine, Bronx, NY.*

4 *Department of Critical Care, McGill University Health Centre, Montréal, Québec, Canada.*

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For information regarding this article, E-mail: david.a.kaufman@nyumc.org

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